UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/599,401	02/27/2007	Seth Hallstrom	16785.10	8352

22913 7590 10/13/2010

Workman Nydegger
1000 Eagle Gate Tower
60 East South Temple
Salt Lake City, UT 84111

EXAMINER	
LIU, SAMUEL W	

ART UNIT	PAPER NUMBER
1656	

MAIL DATE	DELIVERY MODE
10/13/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/599,401	HALLSTROM ET AL.	
	Examiner	Art Unit	
	SAMUEL LIU	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 September 2010*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,7 and 14* is/are pending in the application.

4a) Of the above claim(s) *none* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,7 and 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of claims

Claims 1, 2, 7, and 14 are pending.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/30/10 has been entered.

The amendment filed 9/30/10 which amends claims 1, 2, 7 and 14, and cancels claims 4-6, 8-13 and 15-18 has been entered. Claim 3 was cancelled by the amendment filed 3/16/10. Claims 1, 2, 7, and 14 are under examination.

Withdrawal of objections

[1] The objection of the specification is withdrawn in light of the amendment of the specification thereof.

[2] The objection to claims 1, 2, and 4-18 is withdrawn in light of cancellation of claims 4-6, 8-13, and 15-18 and the amendment of claim 1 (yet, the currently amended claim 1 is under 112/2 rejection, see below).

New-Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 7, and 14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement; this is a new matter rejection. The claims

contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The limitation of "molecular weight 10,000 g/ml", which as amended into the claims on 9/30/10, is not supported in the specification as originally filed. Applicant can either cancel the new matter or point out specification support for the phrase in the specification as originally filed.

New-Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter that the applicant regards as his invention.

Claims 1, 2, 7, and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites "molecular weight 10,000 g/ml" wherein "g/ml" refers to "molar mass" (the mass of a mol of a substance, see "The Mole & Molar Mass" (2010, updated) www.chemteam.info/Mole/MolarMass.html, pages 1-2) which differs from "molecular weight" having unit "daltons". Thus, use "molecular weight" with "g/ml" renders the claim ambiguous. Claims 2, 7 and 154 which do not cure the defect of claim 1 are also rejected.

Maintained-Claim Rejections - 35 USC §103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious

at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 7, and 14 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Schlag et al. (US Pat. No. 6358918 B1) in view of Hallstrom et al. (2002) *Circulation*, 105, 3032-3038).

In patent claims 16-18 and 21, Schlag et al, teach a method of treating an ischemia (cerebral ischemia) comprising administering to a patient in need thereof a pharmaceutical composition comprising at least one (*plurality*) thiol nitrosated (i.e., S-nitroso) thiol-group-containing proteins, wherein "at least one" encompasses more than one S-nitroso-proteins that include S-nitroso-albumin (patent claims 21).

Said pharmaceutical composition may comprise any proteins including a low-molecular weight proteins with free thiol group, e.g., reduced glutathione (col.2, lines 51-52 and 61-62) which molecular weight is less than 10,000", wherein said "any proteins" (plurality) is in mixture form (col.2, line 58). These are applied to instant claim 1.

At least 95% of the thiol-group-containing proteins are S-nitrosated (patent claim 19) while N-nitrosation, O-nitrosation and/or C-nitrosation level is less than 10% (patent claim 24). A Near complete S-nitrosation of albumin is preferred, e.g., > 95% S-nitroso albumin (see patent

claims 16, 17, 19 and 21, and col.3, lines 5-6). These are applied to instant claims 2, 7 and 14.

Provided that Schlag et al. do not expressly disclose or provide working example for combined use of S-nitroso-albumin (S-NO-HSA) and S-nitroso-glutathione (GSH) for treating the ischemia.

Schlag et al., however, teach the increased S-nitrosation level with the higher the "NO-coupled effect" when administering a nitrosated protein preparation comprising such the increased S-nitrosation level (col. 2, lines 23-34), wherein said nitrosated protein is S-NO-HSA (patent claim 21), and wherein the "NO-coupled effect", in the relative art, refers to high level of nitric oxide (NO) production during ischemia followed by increasing release of O_2^- (an oxygen *radial*) thereby increasing endothelial ischemic damage (p.3032, right col., lines 10-14, Hallstrom et al.). The reduced glutathione (GSH) has ability of destructing radials such as "O_2^-" and GSH serves as the first line of defense against tissue injury (ischemia/reperfusion, see abstract, Hallstrom et al.) due to oxygen toxicity caused by said radical (see p.3037, right col., last paragraph, lines 1-10, Hallstrom et al.)

Schlag et al. teach that a near complete S-nitrosation of albumin is preferred, e.g., > 95% S-nitroso albumin (see patent claims 16, 17, 19 and 21, and col.3, lines 5-6). Also Schlag et al. teach use of thiol-group containing proteins (encompassing GSH) for formulating a pharmaceutical composition for treating the ischemia (col.6, lines 56-63).

These teachings are applicable to claim 1 and dependent claims therefrom.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use S-nitroso albumin (S-NO-HSA) and GSH together for treating the ischemia. This is because the S-NO-HSA is a powerful tool in treating or reducing the

ischemia/reperfusion thereof (p. 3038, last paragraph, lines 6-7, Hallstrom et al.), and because GSH is able to destruct the oxygen radials "O_2^-" which causes tissue ischemic damage, and serves as the first line of defense against said damage (see above Hallstrom et al. teaching). In view of that the primary reference Schlag et al. is directed to using S-NO-HSA to treat an ischemia state, upon reading the Schlag and Hallstrom references, one of ordinary skill in the art would have readily recognized benefit of combination of use of GSH and S-NO-HSA to treat the ischemia; said benefit is that both GSH and S-NO-HAS actively scavenge superoxide (O_2^-) which contributes to the ischemic injury or damage. Thus, one of ordinary skill in the art would have tried to formulate GHS with S-NO-HSA into the pharmaceutical composition to treat the ischemia injury or damage. When tried, it would have led to reasonable expectation of success. Therefore, the combination of the references' teachings renders the claimed invention *prima facie* obvious in the absence of unexpected result.

The applicants' response to the 103(a) rejection above

At pages 6-11, the response filed 9/30/10 discusses col.2, lines 61 and 62 in Schlag et al. reference, and submits that Schlag et al. do not teach instant pharmaceutical composition comprising the reduced glutathione (GSH) and *S*-nitrosated albumin; and the response argues that in Schlag's reference, the low-molecular weight GHS is not regarded as the protein(s) but rather a peptide which Schlag et al. use in their pharmaceutical composition for treating ischemia, wherein molecular weight of the proteins of Schlag et al. does not meet instant limitation "10,000 g/ml and less" (p.7, 3rd and 4th paragraphs, and p.8, 1st paragraph).

The response also discuss col.1, lines 48-58, Schlag et al. and asserts that glutathione is not desired (p.8, 2nd paragraph).

Further, the response submits that although Hallstrom et al. reference disclose S-NO-HAS is useful for treating ischemia/reperfusion injury by decreasing production of oxidized

species (O_2^-), the reference teach nothing regarding combination of S-NO-Has with any other compound is indicated or suggested (p.9, 3rd paragraph). Thus, the response infers that none of the prior art alone or in combination teaches/suggests use of both S-NO-HAS and GSH to treat ischemia, and therefore, the response request withdrawal of the rejection above.

The applicants' arguments are found unpersuasive because the reason discussed in the above rejection, and the because of the reasons below.

At col.2, lines 61 and 62, Schlag et al. teach the pharmaceutical composition for treating the ischemia state contain any protein**s** (*plurality form*) with "free" thiol group or "mixtures" thereof; said "protein**s**" encompasses low molecular weight protein e.g., glutathione (GSH) (see col.2, line 61-62), wherein Schlag et al. regard GSH as "protein" not peptide, and wherein GSH has molecule weight below 10,000. Nowhere in col. 1, lines 48-58 of Schlag et al. indicates that glutathione is not desired.

In addition to the treatment of the ischemia reperfusion with powerful compound S-NO-HSA, Hallstrom et al. have taught that GSH is able to destruct the oxygen radials "O_2^-" which causes tissue ischemic damage, and serves as the first line of defense against said damage (see above). Upon reading the Schlag and Hallstrom references, one of ordinary skill in the art would have readily recognized benefit of combination of use of GSH and S-NO-HSA to treat the ischemia, since both GSH and S-NO-HAS actively scavenges superoxide (O_2^-) that contributes to the ischemic injury/damage, and would have modified the composition by formulating GHS with S-NO-HAS for said treatment with reasonable expectation of success. Therefore, the 103(a) rejection above is proper and stands.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samuel Liu whose telephone number is (571)272-0949. The examiner can normally be reached on Monday-Friday, 9 am to 5:30 pro. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Manjunath N. Rao can be reached on 571-272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Samuel Wei Liu/
Patent Examiner, Art Unit 1656
/ANAND U DESAI/
Primary Examiner, Art Unit 1656
October 12, 2010